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66. (New) The isolated polypeptide of claim 8, wherein said polypeptide comprises a calcium binding domain.

67. (New) The isolated polypeptide of claim 66, wherein said calcium binding domain is selected from the group of amino acid residues consisting of

- a) amino acid residues 126-154 of SEQ ID NO:20;
- b) amino acid residues 162-190 of SEQ ID NO:20; and
- c) amino acid residues 210-238 of SEQ ID NO:20.

REMARKS

Claims 8, 10, and 55-65 were pending in the application. Claims 55, 56, 59 and 60 have been cancelled, without prejudice, claims 8, 10, 57, 58, and 61-65 have been amended, and new claims 66-67 have been added. Accordingly, after the amendments presented herein have been entered, claims 8, 10, 57, 58, and 61-67 will remain pending. For the Examiner's convenience all of the pending claims are set forth herein in Appendix A.

Attached hereto is a marked-up version of the changes made to the claims by the current amendments. The attached page is captioned "**Version With Markings to Show Changes Made.**"

Support for the amendments to the claims can be found throughout the specification and in the claims as originally filed. Specifically, support for claims 66 and 67 can be found at page 23, line 30 through page 24 line 22 of the specification.

No new matter has been added. Any cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Objection to the Claims

The Examiner has objected to claims 8, 10, and 55-65 because they contain limitation drawn to non-elected subject matter.

Applicants have cancelled claims 55, 56, 59, and 60 thereby rendering this objection, as it pertains to these claims, moot. Moreover, Applicants have amended claims 8, 10, 57, 58, and

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61-65 to recite only the polypeptides elected in the Response to Restriction Requirement filed August 23, 2002. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing objection. Further, claims 62-65 should be allowable once this objection is withdrawn.

Rejection of Claims 8, 10, and 55-62 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 8, 10, and 55-62 under 35 U.S.C. § 112, first paragraph, because, "the specification, while being enabling for an amino acid of SEQ ID NO:20, does not reasonably provide enablement for an amino acid sequence which is 60%, 90%, [or] 95% identical to SEQ ID NO:20, or an amino acid sequence which comprises at least 15 contiguous amino acids of SEQ ID NO:20." Specifically, the Examiner is of the opinion that

[c]laims 8, 10, and 55-62 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of PCIP9qm. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of PCIP 9qm[.] It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

And further that,

[s]ince the claims encompass variant nucleic acids and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention.

Applicants have cancelled claims 55, 56, 59, and 60 thereby rendering the foregoing rejection, as it pertains to these claims, moot.

Applicants traverse the foregoing rejection as it pertains to claims 57, 58, 61 and 62 for the following reasons. Applicants would like to bring to the Examiner's attention Example 1 of the Revised *Method for the Preparation of a Protein* (hereinafter "Example 1") which provides that a claim directed to variants of a protein having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" with an accompanying specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. § 112, first paragraph for written

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description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that "[t]he single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity." The Guidelines also provide that ***"[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art."***

Similarly, in the present case, claims 57, 58, 61 and 62 are directed to polypeptides encoded by nucleic acid molecules that are at least 90% or 95% identical to SEQ ID NO:19 or polypeptides that are at least 90% or 95% identical to SEQ ID NO:20, wherein the polypeptide is capable of interacting with a potassium channel. As set forth in Example 14 of the *Written Description Guidelines*, the production of polypeptides which contain a 5% variation from a specific sequence is routine in the art. Furthermore, Applicants have disclosed in the instant specification assays for identifying all of the at least 90% or 95% identical polypeptides of SEQ ID NO:20 that are capable of interacting with a potassium channel (see, for example, Example 10 at page 128 of the specification).

In view of the above, Applicants respectfully submit that an ordinarily skilled artisan reading the foregoing teachings in Applicants' specification would have been able to practice the claimed invention using only routine experimentation. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Rejection of Claims 8, 10, and 55-62 Under 35 U.S.C. § 112, First Paragraph

As previously stated, claims 8, 10, and 55-62 under 35 U.S.C. § 112, first paragraph, are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner is of the opinion that

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[t]hese are genus claims. The claims are drawn to an amino acid sequence which is 60%, 90%, 95% identical to SEQ ID NO:20, or an amino acid sequence which comprises at least 15 contiguous amino acids of SEQ ID NO:20. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded SEQ ID NO:20. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the polypeptide of SEQ ID NO:20 is insufficient to describe the genus.

Applicants have cancelled claims 55, 56, 59, and 60, thereby rendering the foregoing rejection, as it pertains to these claims, moot.

With respect to the remaining claims, Applicants respectfully traverse the foregoing rejection for the following reasons.

Claim 8 and Claims Depending Therefrom

Applicants traverse the foregoing rejection as it pertains to claim 8 for the following reasons. In Example 15 of the *Interim Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, First Paragraph Written Description Requirement* the "theoretical specification" discloses a messenger RNA sequence, SEQ ID NO:1, which encodes a human growth hormone. The "theoretical specification" claims antisense molecules that inhibit the production of human growth hormone. The Guidelines provide that

considering the specification's disclosure of (1) *the sequence (SEQ ID NO:1) which defines and limits the structure of any effective molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim* and (2) the functional characteristics of the claimed invention as well as a routine art-recognized method of scrounge for antisense molecules which provide further distinguishing characteristics of the claimed invention, along with (3) the general level of knowledge and skill in the art, one skilled in the art would

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conclude that applicant was in possession of the invention. ***the claimed invention is adequately described. (Emphasis added).***

Similar to Example 15 of the *Interim Guidelines*, the instant specification describes the nucleotide sequence of the nucleic acid molecule of the invention (SEQ ID NO:19) and the amino acid sequence of the polypeptides of the invention (SEQ ID NO:20) ***which define and limit the structure of any nucleic acid or polypeptide fragments such that one skilled in the art would be able to immediately envisage members of the genus embraced by the polypeptide fragment claims***. In particular, the KChIP molecules of the present invention contain, for example, a calcium binding domain (see page 23, line 32-page 24, line 23 of the specification).

Furthermore, as provided in Example 15 of the *Interim Guidelines*, the generation of nucleic acid fragments is *routine*. For example, (as indicated in Example 15 of the *Interim Guidelines*) any specified fragment can be ordered from a commercial synthesizing service.

Moreover, Applicants have disclosed in the specification ***specific*** examples of species falling within the genus of the claimed polypeptide fragments. For example, Applicants disclose the existence of calcium binding domains, e.g., EF domains, that are critical for the function of PCIP molecules (see page 23, line 30 through page 24, line 20 of the specification). Applicants also show in Example 10, that the mutation of specific residues in the EF domains destroys the ability of KChIP polypeptides to modulate Kv4 channel currents (see page 128, line 1 through page 130, line 9 of the specification).

Based on the foregoing, it is evident that Applicants were in possession of the claimed invention at the time of filing.

Claims 57, 58, 61 and 62 and Claims Depending Therefrom

Applicants traverse the foregoing rejection as it pertains to claims 57, 58, 61 and 62 for the following reasons. Applicants, again, would like to bring to the Examiner's attention to Example 14 of the *Revised Interim Written Description Guidelines Training Materials*. This example provides that a claim directed to variants of a protein having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:1 and 95% identical to SEQ ID NO:2" is allowable under the specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. §112, first paragraph for written description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that "[t]he single species disclosed is representative of the genus because all members have at least 95%

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structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity." The Guidelines also provide that "[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art."

Similarly, in the present case claims 57, 58, 61 and 62 are directed to polypeptides encoded by nucleic acid molecules that are at least 90% or 95% identical to SEQ ID NO:19 or polypeptides that are at least 90% or 95% identical to SEQ ID NO:20, wherein the polypeptide is capable of interacting with a potassium channel. Applicants have disclosed in the instant specification assays for identifying all of the at least 90% or 95% variants of SEQ ID NO:20 that are capable of interacting with a potassium channel (see, for example, Examples 7, 8, and 10, beginning at page 125 of the specification and the cell based assays described at page 87, line 29 through page 88, line 20 of the specification). Thus based on the teachings in Applicants' specification, the ordinary skilled artisan would conclude that Applicants were in possession of the claimed invention at the time of filing the instant application.

In view of all of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this section 112, first paragraph rejection.

Rejection of Claims 55 and 59 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 55 and 59 under 35 U.S.C. § 112, first paragraph as, "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner is of the opinion that, "[d]ue to the limitation of 'allelic variant' recited in the claim, a determination of whether the claim as a whole encompasses elements which are not particularly described (e.g., the sequence of the claimed allelic variants) are encompassed by this claim."

While in no way acquiescing to the validity of the Examiner's rejection, and solely in the interest of expediting prosecution, Applicants have cancelled claims 55 and 59, thereby rendering

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this rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 55 and 59 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has also rejected claims 55 and 59 under 35 U.S.C. § 112, second paragraph as, "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner is of the opinion that, "[c]laims 55 and 59 are indefinite in the recitation of the term 'naturally occurring'."

While in no way acquiescing to the validity of the Examiner's rejection, and solely in the interest of expediting prosecution, Applicants have cancelled claims 55 and 59, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 56 and 60 Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 56 and 60 under 35 U.S.C. § 102(e) as, "being anticipated by U.S. Patent No. 6,117,989 (Bandman et al.)." The Examiner relies on Bandman *et al.* for disclosing a calcium binding protein and is of the opinion that "[t]he calcium binding protein disclosed in the '989 patent is 62.3% identical to the amino acid sequence of SEQ ID NO:20, thus claims 56 and 60 are anticipated."

While in no way acquiescing to the validity of the Examiner's rejection, and solely in the interest of expediting prosecution, Applicants have cancelled claims 55 and 59, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

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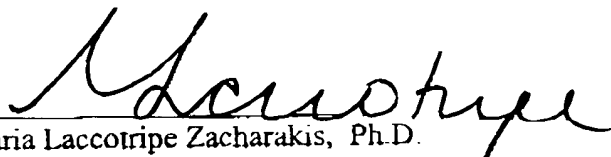
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SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



Maria Laccotripe Zacharakis, Ph.D.

Attorney for Applicants

Limited Recognition Under 37 C.F.R. §10.9(b)

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

8. (Amended) An isolated polypeptide comprising at least 15 contiguous amino acids of the amino acid sequence of ~~SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, or SEQ ID NO:30.~~

10. (Amended) The polypeptide of any one of claims 8, or ~~55-65~~ 57-58, or 61-67 further comprising heterologous amino acid sequences.

57. (Amended) An isolated a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 90% identical to a nucleic acid comprising the nucleotide sequence of ~~SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, or SEQ ID NO:29~~ wherein said polypeptide is capable of interacting with a potassium channel.

58. (Amended) An isolated a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleic acid comprising the nucleotide sequence of ~~SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, or SEQ ID NO:29~~, wherein said polypeptide is capable of interacting with a potassium channel.

61. (Amended) An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of ~~SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, or SEQ ID NO:30~~ wherein said polypeptide is capable of interacting with a potassium channel.

62. (Amended) An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of ~~SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, or SEQ ID NO:30~~, wherein said polypeptide is capable of interacting with a potassium channel.

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63. **(Amended)** An isolated polypeptide comprising the amino acid sequence of ~~SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, or SEQ ID NO:30.~~

64. **(Amended)** An isolated polypeptide consisting of the amino acid sequence of ~~SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, or SEQ ID NO:30.~~

65. **(Amended)** An isolated polypeptide encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number ~~98937, 98939, 98941, 98947, 98948, 98950, 98951, 98991, or 98993.~~

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APPENDIX A

8. An isolated polypeptide comprising at least 15 contiguous amino acids of the amino acid sequence of SEQ ID NO:20.

10. The polypeptide of any one of claims 8, 57-58, or 61-67 further comprising heterologous amino acid sequences.

57. An isolated a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 90% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:19, wherein said polypeptide is capable of interacting with a potassium channel.

58. An isolated a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:19, wherein said polypeptide is capable of interacting with a potassium channel.

61. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:20, wherein said polypeptide is capable of interacting with a potassium channel.

62. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:20, wherein said polypeptide is capable of interacting with a potassium channel.

63. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:20.

64. An isolated polypeptide consisting of the amino acid sequence of SEQ ID NO:20.

65. An isolated polypeptide encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number 98991, or 98993.

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66. The isolated polypeptide of claim 8, wherein said polypeptide comprises a calcium binding domain.

67. The isolated polypeptide of claim 66, wherein said calcium binding domain is selected from the group of amino acid residues consisting of

- a) amino acid residues 126-154 of SEQ ID NO:20;
- b) amino acid residues 162-190 of SEQ ID NO:20; and
- c) amino acid residues 210-238 of SEQ ID NO:20.

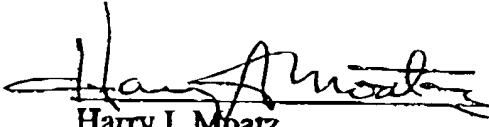
**BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE
UNITED STATE PATENT AND TRADEMARK OFFICE**

LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)

Maria C. Laccotripe Zacharakis is hereby given limited recognition under 37 CFR § 10.9(b) as an employee of Lahive & Cockfield, LLP, to prepare and prosecute patent applications where the patent applicant is the client of Lahive & Cockfield, LLP, and the attorney or agent of record in the applications is a registered practitioner who is a member of the Lahive & Cockfield, LLP. This limited recognition shall expire on the date appearing below, or when whichever of the following events first occurs prior to the date appearing below: (i) Maria C. Laccotripe Zacharakis ceases to lawfully reside in the United States, (ii) Maria C. Laccotripe Zacharakis' employment with Lahive & Cockfield, LLP ceases or is terminated, or (iii) Maria C. Laccotripe Zacharakis ceases to remain or reside in the United States on an H-1 visa.

This document constitutes proof of such recognition. The original of this document is on file in the Office of Enrollment and Discipline of the U.S. Patent and Trademark Office.

Expires: August 5, 2003


Harry I. Moatz
Director of Enrollment and Discipline